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Determination of Optimum Vitamin D Nutrition in Young Women

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13. SUPPLEMENTARY NOTES

14. ABSTRACT
The main objective of the current proposal is to study the effect of increasing doses of vitamin D_3 in a group of young women with hypovitaminosis D (serum 25OHD < 20 ng/ml) and an adequate calcium intake of 1200 -1400mg/day. This is a double blind randomized placebo controlled study .There will be 5 treatment arms, four vitamin D3 dose groups ,400, 800, 1600, and 2400 IU/day and placebo .Calcium citrate tablets will be given to maintain the calcium intake between 1200-1400mg/d in all subjects. The study will recruit up to 100 Caucasian and 100 African American women subjects) between age 25 and 45. The primary outcomes are changes in serum 25OHD and serum PTH. Secondary outcomes are calcium absorption, physical performance tests and safety measurements of serum calcium and 24 hour urine calcium. Subjects will be recruited in the spring and winter seasons of two consecutive years.
In the first winter active recruitment started on April 1 2008 and finished in July 2008 and the first subject was randomized to treatment on 04/28/2008. To date we have 49 subjects randomized to treatment (20 African Americans and 29 Caucasians).

15. SUBJECT TERMS
hypovitaminosis D, vitamin D treatment, RDA

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Introduction

The diagnosis of vitamin D deficiency (serum 25OHD<12ng/ml) and vitamin D insufficiency (serum 25OHD<20ng/ml) have become more common in the last 3 years as health professionals became more aware of this issue. It has been suggested that a serum 25OHD level of 30ng/ml is optimal for bone health because serum parathyroid hormone levels are lower at this level and markers of bone resorption are decreased.
It is also suggested that the RDA (Recommended Dietary Allowance) for vitamin D should use this serum 25OHD level as a goal when estimating the RDA. Because there have been no systematic dose response studies on vitamin D we postulate that the minimal dose of vitamin D that will achieve a serum 25OHD of 30 ng/ml in 97 percent of young women during the winter will exceed 1700 IU/day in Caucasian and 2000 IU/day in African American women. This is much higher than the present RDA of 400-600 IU/day which may need to be revised upwards if this hypothesis is confirmed.
To measure the dose response we will use vitamin D_3 doses of 400, 800, 1600, and 2400 IU/day plus a calcium intake of 1200-1400mg/day compared with a placebo group and similar calcium intake.

Body

Funding for this study started on October 6 ,2007. The first six months involved development of a protocol, construction of subject charts, submission to the local IRB and approval by DOD. There was a significant delay in approval by HRPO

10/6/2006	Award Notice	Pamela Fisle
10/10/2006	Development of protocol and forms	
12/13/2006	Initiate document submission	Amber Stanley
1/25/2007	Protocol submitted to DOD	Dr. Gallagher
9/8/2007	IRB approval of protocol	Dr Gallagher
10/1/2007	Funding started	
10/16/2007	PEF comment	Johanna Kidwell
11/19/2007	Reply to PEF	Dr Gallagher
12/20/2007	PEF further comments	Johanna Kidwell
1/10/2008	PEF further comments	Johanna Kidwell
1/24/2008	Creighton IRB approval of protocol & forms	Dr Gallagher
2/18/2008	UNMC IRB approval	Dr Gallagher
2/19/2008	Study drug arrived	
2/26/2008	DSMB Conference completed. No issues arose.	
3/19/2008	Final approval by HRPO	
3/19/2008	Clinical trial registered NCT00662844	
4/1/2008	Recruitment started	

Recruitment : Because serum 25OHD is lowest in the months January to May we have a restricted window for recruitment .As a result of the delayed approval by HRPO we were only able to recruit for 2 months in the first year- 2008.
Summarizing our activity we screened 786 women on the phone, 216 came in to sign a consent form, 77 qualified on the basis of low serum 25OHD and 49 were randomized to a treatment group. A complete summary of our subject contact and recruitment is shown in table 1 in the appendix. This table illustrates some of the problems and difficulties associated with recruitment. There are losses at all stages but we assume that although 35% qualify on the basis of low serum 25OHD only 22% of those screened will be randomized to study drug. In

order to recruit another 150 women we will need to screen about 750 women this year. The delay in starting last year has increased the burden this year.

Results: The mean serum 25OHD for 163 Caucasian women screened was 27ng/ml and for those who qualified it was 16ng/ml .For 53 African American women the mean for all those screened was 12 ng/ml and for qualifiers was 11ng/ml. Thus, 23 percent of Caucasians and 73 percent of African Americans have vitamin D insufficiency as defined.

Progress of Randomized subjects: 6/49subjects (12 %) have dropped from study, 3 were lost to follow up,2 were non compliant and 1 refused further blood tests.

Key Research Accomplishments
None at this time.

Reportable outcomes
There are no primary outcomes to report yet since we are only 25% recruited. The outcomes to be studied are given below.

Primary outcomes of the study are serum 25OHD and PTH levels at the end of the first year of treatment.

Secondary outcome measures are to study the safety of these doses on -serum calcium and urine calcium

Safety: Serum calcium and 24 hour urine calcium are measured every 3 months. None have developed hypercalcemia or hypercalciuria (> 400mg/24h)
There have been no serious adverse events reported.

Conclusion
This study has insufficient data at this time to draw any conclusions, most of the recruitment will take place in the next 6 months and outcome data will be available in 2010.

References
None.

Appendix - Table 1